

WHAT IS CLAIMED IS:

1. A method of enhancing active agent localization at a target site in a mammalian recipient, which method comprises:

administering to the recipient a first conjugate comprising a targeting moiety and a biotin, whereupon the first conjugate localizes to the target site;

administering to the recipient avidin or streptavidin; and

thereafter administering to the recipient a second conjugate comprising biotin, a linker resistant to biotinidase cleavage and an active agent, wherein second conjugate localization at the target site is enhanced as a result of prior localization of the first conjugate.

2. A method of claim 1 wherein the targeting moiety is proteinaceous.

3. A method of claim 1 wherein the targeting moiety is an oligonucleotide, a peptide, a polypeptide, a cytokine, a monoclonal antibody, a monovalent fragment thereof.

4. A method of claim 3 wherein the monoclonal antibody is a human, a humanized or a chimeric monoclonal antibody.

5. A method of claim 3 wherein the monoclonal antibody or fragment thereof is reactive with an antigen recognized by the antibody NR-LU-10.

6. A method of claim 1 wherein the active agent is selected from the group consisting of

radionuclides, chemotherapeutic drugs, anti-tumor agents and toxins.

7. A method of claim 6 wherein the active agent is a radionuclide selected from the group consisting of Re-186, Re-188, Tc-99m, Y-90, At-211, Pb-212, Bi-212, Sm-153, Eu-169, Lu-177, Cu-67, Rh-105, In-111, Au-198, I-123 and I-131.

8. A method of claim 6 wherein the active agent is a cytokine or a lectin inflammatory response promoter.

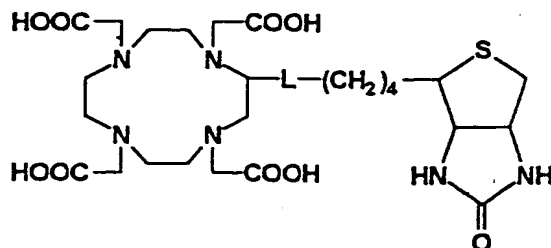
9. A method of claim 1 wherein the step of administering the second conjugate is conducted by intralesional or intraarterial injection.

10. A method of claim 9 wherein the second conjugate is administered via an artery supplying target site tissue.

11. A method of claim 9 wherein the second conjugate is administered via an artery selected from the group consisting of hepatic artery, carotid artery, bronchial artery and renal artery.

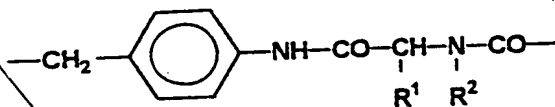
12. A method of claim 1 wherein the second conjugate is administered intravenously.

13. A method of claim 1 wherein the second conjugate comprises a biotin-DOTA compound of the following formula:

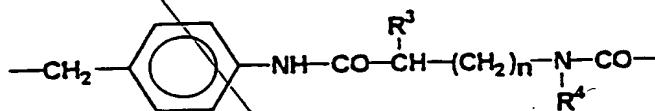


wherein a linker L is selected from the group comprising:

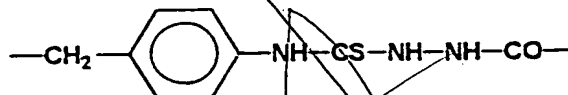
- 1) a D-amino acid-containing linker of the formula



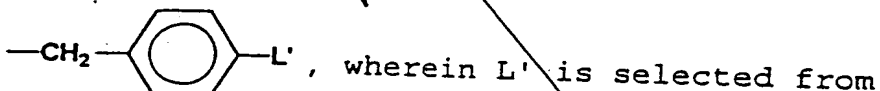
- 2) a linker of the formula



- 3) a linker of the formula



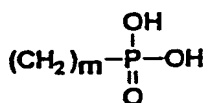
- 4) a linker of the formula



the group comprising:

- a) $\text{---NH---CO---(CH}_2\text{)}_n\text{---O---}$;
- b) ---NH--- ;
- c) $\text{---NH---CO---CH}_2\text{---N---R}^{\prime\prime}\text{---}$;
 R^{\prime}
- d) $\text{---NH---CS---NH---}$; and
- e) $\text{---NH---CO---(CH}_2\text{)}_n\text{---NH---}$,

wherein R¹ is hydrogen, lower alkyl; lower alkyl substituted with one or more hydrophilic groups including (CH₂)_m-OH, (CH₂)_m-OSO₃, (CH₂)_m-SO₃, and



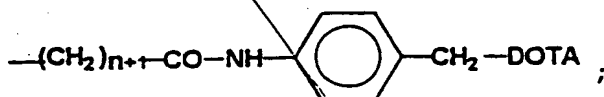
, where m is 1 or 2;

glucuronide-substituted amino acids; or other glucuronide derivatives;

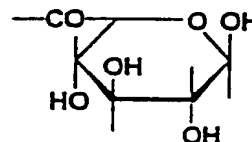
R^2 is hydrogen; lower alkyl; substituted lower alkyl having one or more substituents selected from the group comprising hydroxy, sulfate, and phosphonate; or a hydrophilic moiety;

R^3 is hydrogen; an amine; a lower alkyl; a hydroxy-, sulfate- or phosphonate-substituted lower alkyl; a glucuronide; or a glucuronide-derivatized amino acid;

R^4 is hydrogen, lower alkyl or

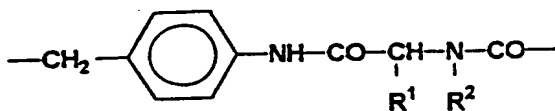


R' is hydrogen, $-(CH_2)_2-OH$ or a sulfate or phosphonate derivative thereof; or



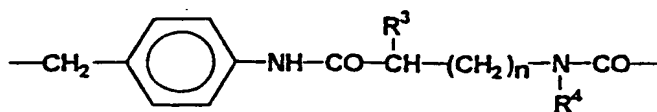
R'' is a bond or $-(CH_2)_n-CO-NH-$; and n ranges from 0-5.

14. A method of claim 13 wherein L is a D-amino acid-incorporating linker of the formula



15. A method of claim 14 wherein R^1 is CH_3 and R^2 is H.

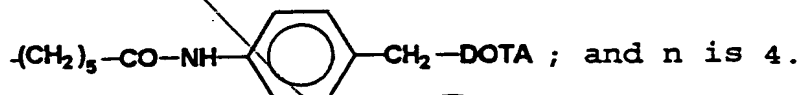
16. A method of claim 13 wherein L is a linker of the formula



17. A method of claim 16 wherein R^3 is hydrogen; R^4 is CH_3 ; and n is 4.

18. A method of claim 16 wherein R^3 is hydrogen; R^4 is CH_3 ; and n is 0.

19. A method of claim 16 wherein R^3 is hydrogen; R^4 is



20. A method of claim 13 wherein L is a linker of the formula



the group comprising:

a) $-NH-CO-(CH_2)_n-O-$;

b) $-NH-$;

c) $-NH-CO-CH_2-\underset{\substack{| \\ R'}}{N}-R''-$;

d) $-NH-CS-NH-$; and

e) $-NH-CO-(CH_2)_n-NH-$ or a bis-DOTA derivative thereof.

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